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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER

CHEN, LIPING

ART UNIT	PAPER NUMBER
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1632

DATE MAILED: 12/16/2002

9

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/762,573

Applicant(s)

REGULIER ET AL.

Examiner

Liping Chen

Art Unit

1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 20 November 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-21, 23 and 24 is/are pending in the application.
- 4a) Of the above claim(s) 6, 8-10, 16-18 and 21 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-5, 7, 11-15, 19, 20, 23 and 24 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 02/08/2001 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☒ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION***Restriction/Election***

Applicant's election with traverse of Group I, claims 1-7, 11-15, 19, 20 23 and 24, in Paper No. 8, is acknowledged. The traversal is on the ground(s) that the pending claims of the present invention all share the same technical feature. This is not found persuasive because according to 37 C.F.R. 1.475, the specific feature is a product, a process specially adapted for the manufacture of the said product, and a use of the said product. Since all the elements: such as MIP, IL-2, protein encoded by suicide genes are well known in the art, and the making and using of MIP, IL-2 and genes encoding suicide protein are well known in the art, the instant invention has no contribution in respect of the manufacture or the use of the composition claimed. The traversal is further on the ground that the Examiner has not shown that a serious burden would be required to examine all the claims. This is not found persuasive because composition comprises different second nucleic acid sequences: such as interleukins, suicide protein, search for any of a second gene does not require a search for any others, and vice versa. Further, Group V contains polypeptide, search for polypeptide does not require search for nucleic acid, and vice versa. Therefore, each invention requires a separate search status. Thus, the requirement is still deemed proper and is therefore made FINAL. Therefore, only Group I is examined in this office action.

Art Unit: 1632

Claims 8-10, 16-18 and 21 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected claims, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 8.

Claims 1-21 and 23-24 are pending and claims 1-5, 7, 11-15, 19, 20 and 23-24 are under current consideration for the species of IL-2. Claim 6 is not examined in this office action as it directed to a non-elected species interferon gamma.

Priority

This is a 371 of PCT/FR00/01559, filed 06/07/2000.

Acknowledgment is made of applicant's claim for foreign priority based on an application filed in France 99 07181 on 08/06/1999. It is noted, however, that applicant has not filed a certified copy of the France application as required by 35 U.S.C. 119(b).

Claim Objections

Claims 23 and 24 are objected to because of the following informalities:

Claim 23 is objected to because there are dash lines in front of claim 23. It is suggested to delete the dash lines.

Claim 24 is objected to because there are dash lines following the claim. It is suggested to delete the dash lines.

Specification

The disclosure is objected to because of the following informalities:

This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

The description of the drawings for Fig. 2, 4 and 6 are objected to because they state "the survival rate of these same mice". It is not clear which group of mice are the same mice to each figure.

The description of the drawings for Fig. 6 is objected to because it states "the following genes: huMIP α ". This is suggested to state "the following genes: huMIP1 α ".

The description of the drawings for Fig. 6 is objected to because it states "adenoviruses expressing the following genes: Tris buffer". It is not clear how can an adenovirus express Tris buffer.

Fig. 2, 3, 5, 6 and 7 are objected to because the contents in the inset are not clear.

Claim Rejections - 35 USC § 112, 1st paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

Art Unit: 1632

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-5, 7, 11-15, 19, 20, 23 and 24 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 1 is directed to a composition comprising (i) a nucleic acid sequence encoding all or part of an MIP chemokine, (ii) at least one nucleic acid sequence encoding all or part of a polypeptide having at least cytotoxic activity; said nucleic acid sequences being placed under the control of the elements required for their expression in a host cell of a mammal; claims 2-5, 7, 11-13 and 23 are further directed to different embodiments; claims 2 and 23 are directed to the MIP of claim 1 is MIP1 (claim 2) and MIP1 α or MIP1 β , respectively; claims 3-5 and 7 are further directed to the peptide having cytotoxic activity of claim 1 is cytokine (claim 3), interleukins (claim 4) or IL-2 (claim 5 and 7); claim 11-13 are directed to composition of claim 1, wherein said nucleic acid sequences are inserted into a recombinant vector of plasmid or viral origin (claim 11), which are in the same vector (claim 12) or distinct vectors (claim 13); claim 14 is directed to a vector comprising the nucleic acid sequences of claim 1, claim 15 is directed to the vector of claim 14 is a viral vector; claims 19-20 are directed formulation comprising the

composition of claim 1 and is pharmaceutically accepted; claim 24 is directed to a method of treating a patient in need comprising administering an effective amount of the composition of claim 1.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111 (Fed. Cir. 1991), clearly states that “applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the ‘written description’ inquiry, *whatever is now claimed*.” *Vas-Cath Inc. v. Mahurkar*, 19USPQ2d at 1117. The specification does not “clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed.” *Vas-Cath Inc. v. Mahurkar*, 19USPQ2d at 1116. In the instant case, while a written description for composition comprising a nucleic acid sequence encoding MIP1 α or MIP1 β chemokine and natural variants of MIP1 α or MIP1 β , and at least on nucleic acid sequence encoding IL-2 (specification page 3, line 30 to page 7, line 2) is generally understood, there is no written description regarding which part of sequences of MIP1 α or MIP1 β or their natural variants or which part of IL-2 that has the activity of the respective full length one or other MIPs. Therefore, with the exception of the MIP1 α and MIP1 β chemokine and their natural variants and IL-2, the skilled artisan cannot envision the detailed chemical structure of any part of each sequences that encoding a part of respective peptide will possess the function that is required for the purpose of cytotoxic treatment in mammal nor other MIPs found in nature or made synthetics. Adequate written

Art Unit: 1632

description requires more than a mere statement that it is part of the invention and reference to a potential method of identifying it. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991). Possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with sufficient relevant identifying characteristics (as it relates to the claimed invention as a whole) such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. *Pfaff v. Wells Electronics, Inc.*, 48 USPQ2d 1641, 1646 (1998).

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence. In the instant case, MIP1 α and MIP1 β chemokine and their natural variants and IL-2 meet the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claims 1-5, 7, 11-13, 19, 20, 23 and 24 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for reducing tumor volume and increasing survival rate of a subject with solid tumors by direct

Art Unit: 1632

injection of a composition comprising MIP1 α or MIP1 β and IL-2 into the tumors, does not reasonably provide enablement for increasing survival rate of a subject with other types of tumors, or treatment of tumors or other diseases in a patient in need. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claim 1 is directed to a composition comprising (i) a nucleic acid sequence encoding all or part of an MIP chemokine, (ii) at least one nucleic acid sequence encoding all or part of a polypeptide having at least cytotoxic activity; said nucleic acid sequences being placed under the control of the elements required for their expression in a host cell of a mammal; claims 2-5, 7, 11-13 and 23 are further directed to different embodiments: claims 2 and 23 are directed to the MIP of claim 1 is MIP1 (claim 2) and MIP1 α or MIP1 β , respectively; claims 3-5 and 7 are further directed to the peptide having cytotoxic activity of claim 1 is cytokine (claim 3), interleukins (claim 4) or IL-2 (claim 5 and 7); claim 11-13 are directed to composition of claim 1, wherein said nucleic acid sequences are inserted into a recombinant vector of plasmid or viral origin (claim 11), which are in the same vector (claim 12) or distinct vectors (claim 13); claims 19-20 are directed formulation comprising the composition of claim 1 and is pharmaceutically accepted; claim 24 is directed to a method of treating a patient in need comprising administering an effective amount of the composition of claim 1.

The specification provides working examples of reducing tumor volume of B6D2 immunocompetent mice implanted with B16F0 (H-2b melanoma) tumor cells (Fig. 1), RENCA (H-2d renal carcinoma) tumor cells (Fig. 3), or p815 (H-2d mastocytoma) tumor cells (Fig. 5) by intratumoral injection of adenoviruses expressing huMIP1 α +IL-2 or huMIP1 β +IL-2, which resulted in an increased mice survival rate for treated mice (specification, page 26, line 29 to page 31, line 20, and Fig. 2, 4 and 6). There is no evidence that intratumorally injecting MIP1 α or huMIP1 β with any other cytokines will result in a similar result. Working examples of the instant invention supports this argument. It is noticed that direct injection of p815 tumor cells implanted in mice with adenoviruses expressing huMIP1 α +muIFN γ does not result in significant tumor volume reducing and associated mice survival rate increasing (Fig. 5 and 6). It is also noticed that injection of hmMIP1 β into implanted RENCA tumor cells results in an increased tumor volume (Fig. 3) and a decreased mice survival rate (Fig. 4) comparing with injection of empty Ad. Moreover, the claims are directed to the use of part of MIP and part of polypeptide having at least cytotoxic activity such as part of IL-2, there is no teaching as which part of MIP and IL-2 have the function of respective full length one. Further, besides directly injecting the transgenes into implanted tumors, the specification does not provide any evidence that using huMIP1 α +IL-2 or huMIP1 β +IL-2 will reduce other types of tumors such as leukemia by system delivery. The specification provides a list of tumors and infectious diseases that are

Art Unit: 1632

the target of the instant invention, and states to use different route of transgene delivery (specification, page 24, line 17 to page 25, line 18). However, the specification does not provide any evidence that delivering of huMIP1 α +IL-2 or huMIP1 β +IL-2 by the route other than direct injection will reduce symptom of any disease or tumor. It is well known in the art that cancer is a result of the accumulation of multiple abnormalities and a result of complex multistep process (Cooper, Oncogenes, Jones and Bartlett Publishers, 1990, page 4, last parag.). Many tumor oncogenes (Cooper, page 76, Table 5.1, page 89, Table 6.1 and page 112, table 8.1) and tumor suppressor genes (Cooper, page 132-135) have been recognized to be related with certain type of carcinomas. There is also evidence that environmental exposure related with cancer formation (Feigelson, et al. J. Cell. Biochem. 25S:15-22, 1996, Abstract). There is no evidence that using huMIP1 α +IL-2 or huMIP1 β +IL-2 will be able to treat different types of tumors and other diseases with all kind of causes. Although the specification demonstrates by using huMIP1 α +IL-2 or huMIP1 β +IL-2 can reduce tumor volume as a result of killing tumor, it is not equivalent to treating a cancer by reversing the pathological process. Further, the specification only provide teaching for intratumoral injection with a dose of 5×10^8 infectious units (specification, page 31, line 1-4), there is no teaching regarding the dose should be used for different administration routes. There is also no evidence that system administration of any adenovirus will result in an effective amount of the cytokines expressing at target site. With regard to

gene therapy, the problems of the lack of efficient delivery systems, lack of sustained expression and host immune reactions has been well recognized in the art (Verma, Nature, 389:239-242, 1997, page 239, col. 1). Rozenberg et al. (S.T.P. Pharma Sciences 11:21-30, 2001) teach that the choice of gene delivery vector is a key factor for the success of gene therapy application (Rozenberg, Abstract). The requirements for a vector to have successful gene delivery include ability to produce high titer vector particles, ability for efficient transgene expression for the desired duration, and low immunogenicity of the vector (Rozenberg, page 21, left col. sec. parag.). Although, the specification demonstrated intratumoral injection of adenoviruses expressing huMIP1 α +IL-2 or huMIP1 β +IL-2 lead to effective results to mice bearing implanted tumors, there is no evidence that different delivery route such as system delivery will result in effective amount of adenoviruses expressing transgene at any target site.

Therefore, in view of the results obtained from the working examples, the inconsistent responses of different implanted tumors to administered cytokines (Fig. 3-6), the lack of evidence that part of huMIP1 α + part of IL-2 or part of huMIP1 β + part of IL-2 will reduce tumor volume of any types, the lack of evidence that huMIP1 α +IL-2 and huMIP1 β +IL-2 will reduce tumor volume of tumors other than solid tumor by different route of transgene delivery, lack of evidence that huMIP1 α +IL-2 or huMIP1 β +IL-2 can reduce symptom of other diseases or treat any disease including tumors, the quantity of experimentation necessary to determine

Art Unit: 1632

huMIP1 α +IL-2 and huMIP1 β +IL-2 for treating any disease, based upon the nature of the invention, the state of the prior art, the complicity in tumor development and causes, the unpredictability in gene therapy, lack of evidence that to use any different cytokines in combination with MIP1 α or huMIP1 β will result in reducing tumor volume in any subject bearing tumors of any sources, the claimed invention would have required one skilled in the art to engage in an undue amount of experimentation without a predictable degree of success to achieve any specific and the breath of the invention.

Claims 14 and 15 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a vector comprising a nucleic acid sequence encoding MIP chemokine and at least one nucleic acid sequence encoding a full length polypeptide having at least cytotoxic activity, does not reasonably provide enablement for a vector comprising a nucleic acid sequence encoding part of MIP chemokine and at least one nucleic acid sequence encoding part of a polypeptide having at least cytotoxic activity. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claim 14 is directed to a vector comprising a nucleic acid sequences encoding all or part of an MIP chemokine, and at least one nucleic acid sequence encoding all

Art Unit: 1632

or part of a polypeptide having at least cytotoxic activity; claim 15 is directed to the vector of claim 14 is a viral vector.

The specification provides teaching regarding a vector comprising a nucleic acid sequence encoding MIP1 α or MIP1 β chemokine and natural variants of MIP1 α or MIP1 β , and at least on nucleic acid sequence encoding IL-2 (specification page 3, line 30 to page 7, line 2). However, there is no teaching regarding which part of sequences of MIP1 α or MIP1 β or their natural variants or which part of IL-2 that has the activity of the respective full length one or other MIPs. Therefore, there is no direction for a skilled artisan to construct a vector expressing peptide or a part of MIP and a part of a polypeptide to have cytotoxic activity. It is well known in the art, a point mutation can cause a protein losing its activity. Due to the lack of the direction for a part of MIP and a part of IL-2 that have the activity of the respective full length one, the claimed invention would have required one skilled in the art to engage in an undue amount of experimentation without a predictable degree of success to achieve the specific of the invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject

Art Unit: 1632

matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-7, 11-15, 19, 20, 23 and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bourns et al. (U.S. Patent 6,287,557 B1, issued 09/11/2001, filed 02/21/1996) taken with Hobaart et al. (U.S. Patent 6,147,055, issued 11/14/2000, filed 03/14/1997) and Nakashima et al. (Pharm Res 13:1896-1901, 1996).

Claim 1 is directed to a composition comprising (i) a nucleic acid sequence encoding all or part of an MIP chemokine, (ii) at least one nucleic acid sequence encoding all or part of a polypeptide having at least cytotoxic activity; said nucleic acid sequences being placed under the control of the elements required for their expression in a host cell of a mammal; claims 2-7, 11-13 and 23 are further directed to different embodiments; claims 2 and 23 are directed to the MIP of claim 1 is MIP1 (claim 2) and MIP1 α or MIP1 β , respectively; claims 3-5 and 7 are further directed to the peptide having cytotoxic activity of claim 1 is cytokine (claim 3), interleukins (claim 4) or IL-2 (claim 5 and 7); claim 11-13 are directed to composition of claim 1, wherein said nucleic acid sequences are inserted into a recombinant vector of plasmid or viral origin (claim 11), which are in the same vector (claim 12) or distinct vectors (claim 13); claims 14 is directed to a vector comprising the nucleic acid sequences of claim 1, claim 15 is directed to the vector of claim 14 is viral vector; claims 19-20 are directed formulation comprising the composition of claim 1 and is pharmaceutically accepted; claim 24 is directed to a

Art Unit: 1632

method of treating a patient in need comprising administering an effective amount of the composition of claim 1.

Boursnell et al. ('557) teach mutant virus vectors encoding nucleotide sequences expressing useful immunomodulating proteins including cytokines and chemokines ('557, col. 6, line 55-67), such as IL-2, MIP1 α and MIP1 β ('557, col. 7, line 1-11) for cancer immunotherapy ('557, col. 11, line 8-11), where each of the heterologous nucleotide sequences can be placed under the control of any of a wide variety of known viral promoters or under the control of a known mammalian tissue-specific promoter ('557, col. 9, line 45-51) (pertaining to instant claims 1-5, 7 and 23). Boursnell et al. further teach that two or more nucleotide sequences can be encoded within one virus vector or a mixture of two or more vectors containing at least one gene encoding a different immunomodulator product can be used ('557, col. 8, line 50-55, pertaining to instant claims 11-15). Further Boursnell et al. teach the method of using the mutant virus vector for cancer immunotherapy for a human or non-human animal subject by either direct or indirect administration (col. 11, line 8-67) (pertaining to instant claim 24). The vectors used in the therapy by Boursnell et al. are formulation, which is pharmaceutically accepted (pertaining to instant claim 19-20). However, Boursnell et al. ('557) does not provide working example for using nucleotide encoding IL-2 or MIPs for reducing tumors.

Hobart et al. ('055) teach introducing plasmid expressing of IL-2 into solid tumor nodules for immunotherapeutic treatment of patients ('055, col. 4, line 33-41,

Art Unit: 1632

line 66 to col. 5, and col. 33, line 33 to col. 36, line 37). Hobart et al. ('055) cure the deficiency of Boursnell et al. ('557) in that it provides evidence of using nucleotide sequence encoding IL-2 for the treatment of solid tumor.

Further, Nakashima et al. teach that reduced tumorigenicities in BALB/c mice inoculated with adenocarcinoma cells (Nakashima, page 1896, right col. third parag.) transfected with plasmid encoding human MIP1 α (hu-MIP1 α) or mouse MIP1 α (mu-MIP1 α) resulted in no tumor growth in some mice (Nakashima, page 1897, left col. last parag., right col. first full parag. and page 1898, Table II). Histological analyses demonstrate predominantly infiltration of macrophages and neutrophils as well as necrotic destruction within tumors expressing hu-MIP1 α or mu-MIP1 α (Nakashima, page 1899, Fig. 1). Further, tumor free mice resulted from inoculation of tumor cells expressing hu-MIP1 α , show rejection to a second inoculation with parental tumor cells that do not express hu-MIP1 α (Nakashima, page 1900, Fig. 4). Therefore, Nakashima et al. conclude that hu-MIP1 α may be of potential value for cancer gene therapy (Nakashima, page 1900, right col. sec. parag.). Nakashima et al. cure the deficiency of Boursnell et al. ('557) in that it provides evidence that MIP1 α gene can be used for the treatment of certain tumors.

One of skill in the art of tumor gene therapy would be motivated to combine the teachings of Boursnell et al. ('557) with the teaching of Hobart et al. ('055) and Nakashima et al. because both Hobart et al. ('055) and Nakashima et al. provide evidence of using nucleotide encoding IL-2 and hu-MIP1 α , respectively, to achieve

Art Unit: 1632

reducing tumor effects. Therefore, at the time the invention was made it would have been *prima facie* obvious to use the system taught by Boursnell et al. ('557) to combine the tumor reducing effect of IL-2 and hu-MIP1 α by construction a composition comprising nucleotide sequences encoding IL-2 and hu-MIP1 α taught by Hobart et al. ('055) and Nakashima et al. to achieve a reasonable expectation of success.

Thus, the claimed invention, as a whole, is clearly *prima facie* obvious in the absence of evidence to the contrary.

Conclusion

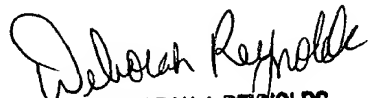
No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Liping Chen, whose telephone number is (703) 305-4842. The examiner can normally be reached on Monday through Friday from 8:00 to 5:00 (Eastern Standard Time). Should the examiner be unavailable, inquiries should be directed to Deborah Reynolds, Supervisory Primary Examiner of Art Unit 1632, at (703) 305-4051. Any administrative or procedural questions should be directed to Dianiece Jacobs, Patent Analyst, at (703) 305-3550. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center

Art Unit: 1632

located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703) 308-8724.

Liping Chen, Ph.D.
Patent Examiner
Group 1632


DEBORAH J. REYNOLDS
SUPERVISORY PATENT EXAMINER
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